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## cancer complex

There are those (and they are invariably doctors) who say the program of cancer public education has overshot the mark—that cancerophobia is resulting and that fear of cancer is reducing many, too many, otherwise healthy people to a state of paralyzed panic. Assuming that the psychiatrists would know a good deal about such things, the American Cancer Society polled a 10 per cent sample of the Diplomates of the American Board of Psychiatry and Neurology, asking their opinions as to the effect of cancer propaganda on the national psyche.

The primary object was to determine the nature and extent of psychiatrists' criticism of cancer publicity and educational material. Among the 272 who replied, only thirty-one felt that current cancer publicity tends to frighten rather than to educate—that the good, if any, does not compensate for the harm done the lay public—and even here the criticism was frequently of health-education methods in general rather than of cancer propaganda

*The Silver Medal of the American Cancer Society is awarded annually for outstanding service in cancer control. In 1950, it was presented to Dr. Clarence C. Little, Director of the Roscoe B. Jackson Memorial Laboratory, in appreciation of his arduous and original studies of genetic factors in cancer, of his development of strains of genetically pure laboratory animals, and for his efforts in cancer control from 1929 to 1945, when he was Managing Director of the American Society for the Control of Cancer.*

*The background of the medal is the traditional academic insignia of the medical profession—the hood of the Doctor of Medicine.*

specifically. Most of the remaining 241 expressed either positive or qualified approval. One hundred seventeen believed that the program does no harm, and most of these imply that it does accomplish some good. Another sixty, by their comments, showed that they were in general agreement with these 117, although they expressed no definite opinion or felt that they weren't qualified to judge. Forty-four felt that the benefits resulting from earlier diagnosis of cancer definitely outweighed any harm done. And, finally, twenty-one were unwilling or unable to pass judgment. All this seems to warrant the conclusion that any harmful effects of cancer publicity are not so serious as the more extreme critics would have us believe.

Perhaps of even greater significance were the unsolicited comments from many of the respondents, pointing out that unwarranted fears, anxieties, and neurotic attitudes are not caused by anything so superficial as health information—but *always* have deep psychological determinants. "The person who fears cancer abnormally," said one psychiatrist, "is bound to fear something, and if it were not cancer, it would be the atomic bomb or insanity or heart disease or any other handy hazard." Which is another way of saying that *balanced* people are *not unbalanced* by cancer propaganda.



# NEWSLETTER

JANUARY 1951

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Experiences with ACTH and cortisone, particularly in treatment of cancer and in animal experimentation, were reported by about seventy investigators at the Conference on the Investigative and Clinical Aspects of ACTH and Adrenocortical Steroids in Neoplastic Diseases, the scientific program of the Annual Meeting of the American Cancer Society, Inc., held in New York City, October 28 and 29. The discussion covered the physiological and pathological changes induced, remissions and relapses, subjective and objective responses, and the side effects that ensued when these steroids were used in the treatment of cancer.

Dr. Sidney Farber, of Boston, who summarized the reports at the end of the Conference, concluded with these words: "The final statement that is certainly permitted on the basis of the work of everyone who has spoken at this meeting is that ACTH and cortisone used alone or used in conjunction with other antitumor substances form an extremely important chapter in the history of clinical investigations in the treatment of incurable cancer. More than that, the investigative tool, now placed in our hands, is one that must be used as actively, as rapidly, and as intelligently as possible on the basis of all the information and research that has come to us from people in our disciplines and other fields of medicine, so that we may find out whether these steroid hormones, or whether compounds much more fundamental in nature than these, perhaps will be of truly curative value in the problem of cancer which is now incurable by present methods of treatment."

\* \* \*

Much of cancer research may never reach the stage where it is front-paged in the public press and starts a stampede

to the doctor's office for new wonder drugs. For your information, however, here's a brief account of some of the current work that may make future news items:

Hormones: HARVARD cancer people are interested in metabolic effects of intermedin, from the posterior pituitary, which seems to check water excretion without increasing the output of sodium chloride--also relaxin, the late pregnancy ovarian hormone. RUTGERS is investigating suppression of rat-liver tumors with thiouracil. CHICAGO is studying the effects of ACTH, cortisone, and other hormones on precancerous lesions. TUFTS and TULANE report good palliative results in metastatic breast cancer with methyl-androstenediol, a nonvirilizing male hormone.

NEW YORK U. investigators, de Bodo, Kurtz, Ancowitz, and Kiang, have found that purified pituitary growth hormone exerts a very potent anti-insulin action and produces a diabetic state in hypophysectomized dogs. Continued administration abolishes the exaggerated hypoglycemic response to insulin.

Money and others at MEMORIAL CENTER, N. Y., have tested effects of adrenal and gonadal products on the radioiodine uptake by rat thyroid. They found, tentatively: Testosterone, progesterone, and estrone increased uptake; estradiol benzoate, ACTH, cortisone, and epinephrine decreased uptake; formalin had no influence. More studies are necessary.

U. of ROCHESTER scientists have found that, at first, testosterone increases nitrogen storage and stimulates growth of genital and other tissues. Protracted administration brings about loss of body fat and transfers nitrogen to sex organs.

Cancer Detection: MASS. INST. TECH. and MASSACHUSETTS GENERAL scientists have a safe method of detecting brain tumors with ultrasonics, and they are exploring the practicability of using radioactive phosphorus and potassium as a diagnostic tool in some kinds of cancer. Their method of using serum albumin to float cancer cells atop

(Continued after page 68)



# Ca

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# KEEPING UP WITH

Digests from current literature of special importance  
in diagnosis and treatment . . .

## Effects of Triethylene Melamine

Therapeutic results similar to those produced by the intravenous injection of the nitrogen mustard HN2 have been induced in some cancers as well as in leukemias and Hodgkin's disease by the oral administration of triethylene melamine. The advantages over HN2 are that it can be administered orally (hence is useful in the ambulant patient), nausea and vomiting are infrequent and preventable, and prolonged dosage control is less difficult. Its effect may be slower, so when rapid control is desired, HN2 is preferable. On the other hand, the toxic effects are identical with those of HN2 so that its oral use must be carefully controlled.

Triethylene melamine (available in scored 5-mg. tablets) is taken with half a glass of plain water immediately on awakening, with breakfast withheld for one hour. Nausea and vomiting—which may occur six or more hours later and last one or two days—may be avoided by regulating the dose to an amount that can be tolerated, ranging from 2.5 to 5 mg. The initial course is 5 to 10 mg. One week later, if the leukocyte count is not altered, another course of 5 to 10 mg. is given. The patient is seen each week and further dosage decided on the basis of the leukocyte count, the hemoglobin, and the clinical condition of the patient. If in three to four weeks, there is no improvement, and moderate leukopenia and anemia have ensued, it is unlikely that any benefit will result.

Four cases of lung cancer were treated. In three, the patients were in

relapse and unsuited to further irradiation; in two, the treatment was ineffective. In the third case, the patient has maintained his general condition; at the time of report, he had received 150 mg. in 93 days; he had had only moderate nausea and vomiting and no hematological toxicity. The fourth case also showed no improvement. Since HN2 has been found to produce symptomatic and objective improvement in the anaplastic or oat-cell variety of lung cancer, it seems likely that triethylene melamine will have a similar effect in suitable cases.

*Karnofsky, D. A.; Burchenal, J. H.; Armistead, G. C., Jr.; Southam, C. M.; Bernstein, J. L.; Craver, L. F., and Rhoads, C.: The use of oral and intravenous triethylene melamine, a compound with nitrogen mustard-like activity, in the treatment of neoplastic disease. To be published.*

## Nitrogen Mustard Yields Palliation in Lung Cancer

Although today surgical removal of carcinoma of the lung offers the only possibility of cure, about 70 per cent of patients are beyond curative resection when first seen by the thoracic surgeon. For some of these, palliative resection can be performed; for the others, some form of palliation by chemotherapy or roentgen rays is necessary.

In this series of sixty patients given nitrogen mustard, two-thirds experienced moderate to excellent subjective relief and about half showed objective evidence of improvement. The latter were related to the histological type of the tumor in the order: undifferentiated, 83 per cent; squamous type, 50

# CANCER

per cent; adenocarcinoma, 33 per cent; and epidermoid carcinoma, 11 per cent. Although results could not be related to dosage, many, not improved by the usual doses, did improve on larger ones.

The dosage most frequently employed was the usual: 0.1 mg. per Kg. of body weight, repeated for four days. Since results seemed to vary from patient to patient, dosages were altered, so that some received the 0.1-mg. doses up to eight days until a relative lymphopenia was noted. According to the patient's weight, the total doses on this schedule varied from 10 to 55 mg. In others, regardless of weight, the patient was started with a 4-mg. dose, and this increased daily until there was actual depression of the leukocyte count. In this group, as much as 3.0 mg. per Kg. was given, or a total up to 180 mg. (Leukocyte and differential counts were done before treatment, daily during, and then for two or three weeks afterward.)

Nausea and vomiting occurred in about one fourth of the patients and was not related to the size of the dose of nitrogen mustard; loss of appetite beyond the period of treatment also occurred in one fourth of the patients and somewhat more frequently among those receiving higher doses. Bone-marrow and leukocyte depression were, however, definitely related to the size of the dose—and to the success of treatment: 89 per cent of those in which the white-cell count fell below 5000 had good or excellent results; only 43 per cent of those who had no fall in white count showed equally good results.

Objective improvement was evidenced by decrease in sputum and in size of primary tumor, metastatic nodes,

and bone metastases; relief of venacaval syndrome; disappearance of convulsions and hemiplegia; cessation of massive hemoptysis; and clearing of atelectasis and pleural effusions. Subjective improvement included decrease in cough, wheeze, and dyspnea; decrease or disappearance of chest pain; increased strength, ambulation, appetite, and well being; loss of pain from bone metastases; and decreased headache.

Although nitrogen-mustard treatment resulted in no average prolongation of life, certain individuals undoubtedly lived longer than they would have otherwise.

*Lynch, J. P.; Ware, P. F., and Gaensler, E. A.: Nitrogen mustard in the treatment of inoperable bronchiogenic carcinoma. Surgery 27: 368-385, March, 1950.*

## Results of Lung-Cancer Therapy at a VA Hospital

All of the 1205 patients with carcinoma of the lung were men, of an average age of 43.2 years. Chest pain and cough were the most frequent symptoms and had been present for an average of seven months before hospitalization.

No etiological factors could be found to account for the increasing incidence of primary carcinoma of the lung at the VA hospital, Hines, Ill., from 2.1 per cent in 1931 to 11.7 per cent in 1946, making lung cancer one of the most frequent of all primary malignant neoplasms.

The relief of symptoms following palliative resection of bronchogenic carcinoma in the forty-nine of 1205 patients regarded operable far exceeded that obtained by any other treatment. Those who survived their first year (26.5 per cent) generally

had a good chance for continued survival. This somewhat lower percentage of operable lesions is probably due to the fact that inoperable cases are sent to the Hines hospital for palliation, while early resectable lesions may be treated at other VA hospitals.

Palliation, although no cures, was obtained from roentgen-ray therapy in the 816 patients treated, and prolonged survivals were achieved in some. Of those treated after 1942, 200 patients received only 300 to 4500 r because of the critical condition in which they were received; they lived about one month after treatment. The eighty patients who received 5000 to 6000 r lived an average of four and a half months; and the sixty who were treated with more than 6500 r lived a little more than four months. Palliation was also experienced by sixty-three who received irradiation for extrathoracic metastases, but they lived less than two months longer. The 241 patients who were given deep roentgen-ray therapy only lived two weeks after treatment ended; it is questionable that such terminal patients should have been treated.

Cases treated before, and those after, 1942 had a parallel survival rate, indicating that the extent of the disease is the predominant factor in longevity, not modern concepts of irradiation.

Ariel, I. M., Avery, E. E.; Kanter, L.; Head, J. R., and Langston, H. T.: *Primary carcinoma of the lung; a clinical study of 1205 cases. Cancer* 3: 229-239, March, 1950.

### **Roentgen-Ray Therapy in Lung Cancer**

Unfortunately, lung cancer is often clinically silent in its earlier stages, so that it is usually discovered accidentally in roentgenograms or in the study of some complication. In this English study, cough was the most common first symptom, followed by pain, dyspnea, lassitude, hemoptysis, wasting, fever, etc. Differential diagnosis is complicated by the fact that lung cancer

may simulate other conditions. "Delayed resolution" and "unresolved pneumonia" should always be regarded as caused by carcinoma unless proved otherwise. All cases of chronic abscess should be carefully studied. Sudden bronchiectasis and rapid clubbing of the fingers are other possible signs.

Contraindications to exploratory thoracotomy—the recommended treatment in all cases when possible—include dissemination, bad general condition of the patient or advanced age, extension of the growth too close to the carina or into the mediastinal viscera, gross widening or distortion of the carina, poor cardiorespiratory reserve, emphysema, and arteriosclerosis, especially coronary insufficiency. Diaphragmatic palsy, empyema, blood-stained effusion, and invasion of the parietal pleura do not necessarily imply an inoperable lesion.

In the presence of such obvious contraindications or refusal to undergo operation, roentgen-ray therapy often gives great symptomatic and radiological improvement. Two of 132 patients treated with roentgen rays have lived for five years compared with five of sixty-two alive for five or more years after pneumonectomy.

The radical course is given to all inoperable cases; to those who refuse operation; to all undifferentiated carcinomas whether operated on or not; and to all in whom cancer is found in the lymph nodes at operation. The course extends over five or six weeks. The dosage for undifferentiated carcinoma is 4500 r, 5500 r for the epidermoid. Four or five fields are used: lateral, anterior, and posterior. Nausea and sickness may often be controlled by pyridoxine (vitamin B<sub>6</sub>). Oral sepsis and anemia are corrected in advance, and the red-blood-cell count should be maintained as far as possible, being checked repeatedly during the course. For palliation, a course of 2500 to 3000 r is given in three weeks. For mediastinal obstruction, 500 r is given

in one dose, supplemented as indicated by the patient's progress.

For palliative treatment, morphine and cocaine in increasing doses with alcohol will afford relief from pain. More severe pain may require intervertebral anesthetics or even cordotomy or division of the phrenic nerve. Osteotomy and curetting may be needed for the intense pain of secondary bony deposits. The suffocative symptoms of mediastinal compression can usually be relieved by roentgen-ray therapy. Pneumonectomy offers palliation, especially in cases of pseudohypertrophic pulmonary osteoarthropathy and where pulmonary infection is causing distress.

Mason, G. A.: *Cancer of the lung; review of a thousand cases.* *Lancet* 2: 587-591, Oct. 1, 1949.

#### **Effect of Interstitial Radiation at Thoracotomy**

When lesions are deemed inoperable at thoracotomy, interstitial irradiation spares the patient the prolonged, rigorous course of external-radiation therapy. Definite palliation—but not significantly prolonged life—resulted in seventeen patients. In this series, the choice of radon needles to obtain better distribution and the use of larger doses were the essential differences from the techniques previously described by other authors.

An attempt was made to provide from six to ten threshold erythema doses to all parts of the neoplasm, with total dosages varying from 2,660 to 15,864 mc.-hr. The active lengths of the three types of radon seeds and needles used were 1, 2, and 4 cm., with an over-all diameter of 0.7 mm. and an 0.3-mm. thick wall, and containing an average of 1, 2, and 4 mc. of radon respectively. By means of ordinary radon-seed inserters, the large needles are permanently planted around the lesion, and the smaller tubes and seeds dispersed throughout the neoplasm.

Care must be exercised in the insertion of the 4-cm. needles not to penetrate an adjacent bronchus or vessel. This accurate distribution is frequently difficult, if not impossible, because of the proximity of the neoplasm to vital structures and the difficulty in differentiating the neoplasm itself from the induration of the pneumonitis that so often surrounds it.

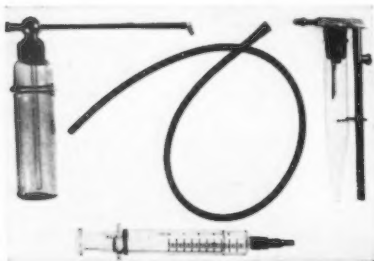
Patients enjoyed prompt though transient (one- to ten-months') palliation, as evidenced by marked diminution in severity of coughing and amount of expectoration; diminished chest pains; reduction in bronchial obstruction to the point of almost complete patency and relief of the atelectasis caused by the obstruction; and abatement of general symptoms such as fever and malaise, with improvement of appetite and gain in weight. In one patient, the size of the tumor decreased from 6.5 to 3.5 cm. in diameter in one month, and this patient is alive and asymptomatic ten months following therapy. The other sixteen patients succumbed on an average of five and a half months following irradiation.

The disadvantages are that overlapping fields may result in overdosage, so that hemoptysis, necrosis, hemorrhage, and activation of a tuberculous lesion may, in some instances, result. Also, because the implanted seeds and needles may not deliver an adequate dose, a study is being made on supplementing the interstitial radiation with a course of deep roentgen-ray therapy. Since it is difficult to distribute the seeds and needles accurately, the method should not be used if surgical cure seems possible, or if a lesion is small and inoperable because of its location—carina, for instance; for the latter, external irradiation is the method of choice. Multiple pulmonary or pleural metastases are contraindications.

Ariel, I. M.; Head, J. R.; Langston, H. T., and Avery, E. E.: *The use of interstitial radon seeds and needles in inoperable lung cancer.* *Cancer* 2: 581-586, July, 1949.

### Tracheal Aspiration Aids Diagnosis

When bronchoscopy is not practical, tracheal aspiration is proving a safe, reliable, and relatively inexpensive method of collecting a specimen for diagnosis in cancer of the lung. The ease of tracheal catheterization is well known. After medication with sodium phenobarbital (gr. 2, intramuscularly) forty-five minutes previously, a 1 per cent pontocaine solution is sprayed (using a DeVilbiss power spray) on the external nares, oropharynx, nasopharynx, hypopharynx, the cords, and subglottic areas. After ten minutes a No. 14 or 16 French rectal catheter moistened with saline (not jelly lubricants) is passed through the patent side of the nose and advanced into the trachea (the patient cranes his neck forward with chin up and breathes freely, while the examiner maintains traction on the tongue). A sterile 10-cc. syringe con-



taining the dilute solution of equal parts of 1 per cent pontocaine and 0.85 per cent saline is attached to the catheter, and 2 cc. of the solution is slowly dropped into the trachea. After a brief period of coughing, the catheter is gently advanced down to the carina region. Irrigating and aspirating repeatedly with a Clerf cancer-cell collector, using 2 cc. of solution each time, a total of 10 cc. of solution is injected. The catheter tip is intermittently manipulated up and down in the tracheo-bronchial tree while the patient coughs repeatedly. As the catheter is withdrawn, suction is stopped to prevent contamination, then flushed with saline to get all the specimen. The specimen is then mixed with an equal quantity of 95 per cent alcohol and bottled.

*The patient is instructed not to eat or drink for two hours.*

If topical anesthesia has been properly performed, tracheal aspiration is well tolerated by the patient, and the cost and risk is minimal in comparison to bronchoscopy. Moreover, a richer, purer, more uniform microscopic picture was obtained by tracheal aspiration in a study of forty-two patients. In all cases the tracheal aspirate improved upon the ratings of the other cytological specimens, although a final diagnosis had not yet been made in twenty-three patients in the series.

*Cahan, W. G., and Farr, H. W.: Tracheal aspiration — an additional method for the early diagnosis of carcinoma of the lung; a preliminary report. Cancer 3: 475-480, May, 1950.*

### Lung Cancer and Coexistent TB

Coexistent bronchogenic carcinoma occurs in 1.5 per cent of pulmonary-tuberculosis cases. All of the eleven reported here occurred in men, whose average age was 54 years; one case of coexistent bronchial adenoma in a 42-year-old woman is included. Six were diagnosed as far-advanced bilateral pulmonary tuberculosis, five as carcinoma. Had a second major disease been suspected, the correct diagnosis could



have been made in six of the eleven; there were no clues to it in the other five.

Chest pain was present in eight, in six on the side of the carcinoma. Severe or prolonged chest pain in the patient with pulmonary tuberculosis points to a possible coexistent bronchogenic carcinoma. All patients had a productive cough, none had gross hemoptysis, and only one, blood-tinged sputum. Five had negative sputum, which does not exclude tuberculosis in cases of co-existent lung cancer. Multiple sputum examinations should be made when bilateral lung infiltrations are found in the roentgenogram. Neither endobronchial tumor nor obstruction was found in the five who were bronchoscoped. Clubbing of the fingers occurred in only two.

The tuberculous process was activated in three of four given roentgen-ray therapy.

The authors conclude that bronchogenic carcinoma is not antagonistic to pulmonary tuberculosis; indeed, the general debility and local obstruction resulting from the tumor may give impetus to the tuberculosis. Neither can any causal relationship be found between the two; either may precede the other.

*Robbins, E., and Silberman, F.: Coexistent bronchogenic carcinoma and active pulmonary tuberculosis. Cancer 2: 65-97, Jan., 1949.*

### **Early Cancer Detection Available in the Physician's Office**

Twenty-eight cases of proved cancer among forty-seven suspicious cases were found by routine cytological examination of 1721 patients, the majority of whom came to physicians' offices for a general physical examination, rarely because of a suspicion of cancer. Most of the smears were of fluid taken from the vaginal vault, but some came from aspiration biopsy of the breast or from secretion from the nipple. Of the forty-seven smears first reported positive, twenty-six were confirmed by biopsy or curettage: thirteen

cases of squamous-cell carcinoma of the cervix; ten of adenocarcinoma of the corpus; and three of carcinoma of the breast. Of the other twenty, eight were reported negative by biopsy or curettage, one was a false positive because of irradiation effect (negative clinically and on biopsy), and two diagnoses were confirmed by other cytologists, although the patients could not be followed up; no follow-up was possible on the other ten.

Thus cytological smears taken routinely in an office practice can be a valuable aid in the early detection of cancer, since the ease, rapidity, and relatively low cost make the method practical. And it would seem to warrant that the physician and patient have such a laboratory diagnostic service available to them.

*Kaufmann, W., and Fiege, H. R., Jr.: Cytologic diagnosis of malignant disease in a general office practice. Surg., Gynec. & Obst. 90: 451-454, April, 1950.*

### **Operability Rate is Double in Terminal Bronchiolar Carcinoma**

Terminal bronchiolar carcinoma of the lung seems to be more amenable to surgical excision—the operability rate (88 per cent) in a series of twenty cases being more than double that of the usual type of lung cancer. Moreover, of the twenty cases from Memorial Hospital, New York, the only five-year survivors were treated surgically.

Pain and cough were the most common presenting symptoms, averaging nearly four months in duration. Three cases displayed no symptoms and were discovered at routine roentgenographic examination. Clinical diagnosis was made in nine cases by a combination of tests: cytological sputum studies in two, aspiration biopsies of lung masses in four, and thoracotomy with biopsy or aspiration biopsy in three patients. In five others, clinical data pointed to a lung tumor.

Nine patients received definitive surgical therapy, of whom five are living—

two as five-year survivors. These had early, low-grade malignant tumors; one underwent lobectomy and the other, simple excision. Pneumonectomy was required in five patients, three of whom died in seven, nine, and nineteen months after operation. One surviving patient was treated by segmental resection of the primary tumor and interstitial radon therapy to the metastatic mediastinal nodes. In only one patient was the tumor found inoperable at the time of thoracotomy—he had direct extension of the tumor to the mediastinum.

The six cases that were treated symptomatically because of the extent of the disease ran a very rapid course.

No appreciable palliative effect was noted in the five patients who received primary radiation therapy, and all died within four to eight weeks after completion of therapy. They were, however, inoperable by present criteria of operability and thus clinically far advanced.

Smith, R. R.; Knudson, K. P., and Watson, W. L.: Terminal bronchiolar or "alveolar cell" cancer of the lung; a report of twenty cases. *Cancer* 2: 972-990, Nov., 1949.

### Myogenic Lung Tumors Show Characteristic Roentgen-Ray Pattern

A characteristic roentgenogram of myogenic tumor of the lung emerges from a study of roentgen-ray findings in seven cases at Memorial Hospital, New York. The authors summarize: "In our experience muscle tumors of the bronchial tree, whether benign or malignant, show roentgenologically a homogeneous, essentially spherical mass of water density, with clear distinct edges. The tumors are single, are usually free in the lung, and average 6 cm. in diameter. They show bronchial displacement with narrowing and infrequently they may be entirely intraluminal. Both benign and malignant forms may reveal enlargement over a period of six to twelve months, and there is no way of dependably distin-

guishing roentgenologically between the two, unless one should see distant metastases. None of our cases showed metastases, effusion, adenopathy, or bone change."

Certain conditions sometimes simulate myogenic lung tumors so closely that diagnosis is impossible. Sometimes they may be ruled out on other grounds. Usually, however, they have certain dissimilarities. Bronchogenic carcinoma of the nodular type may be differentiated by less-well-defined borders, hilar or mediastinal adenopathy, pleural reaction, rib erosion, and faster growth rate. The solitary cancer metastasis (and similarly sarcoma metastasis) usually develops only after its source is recognized. A tuberculoma tends to be smaller, oval, occasionally multiple, and may have a slightly lobulated configuration. A central radiolucence or irregular central calcific deposits are other important clues. Bronchial adenomas have a tendency to occur near the hilus, frequently accompanied by atelectasis and similar complications. These average 3.5 cm. in diameter, are round or oval, and contain no calcification. Hamartomas are distinguished by calcification. Most cysts are readily identified by a sharp border, oval configuration, and their usual relationship to the mediastinum. In dermoid cysts, the presence of calcification and teeth, and the anterior mediastinal position are other dependable points. Pleural mesothelioma usually causes little difficulty because of its location, the accompanying pleural reaction, and the different configuration marked by a base along the pleural surface.

Because all of these are sometimes indistinguishable from muscle tumors, reliable diagnosis can only be made by histological study. The possibility should always be considered, however, when this shadow pattern is encountered.

Sherman, R. S., and Malone, B. H.: A roentgen study of muscle tumors primary in the lung. *Radiology* 54: 507-515, April, 1950.

## Diagnosing Lung Cancer Early

Routine roentgenographic chest studies of patients with chest symptoms will avoid the misdiagnosis of lung cancer as pulmonary tuberculosis, virus pneumonia, bronchitis, asthma, bronchiectasis, or a chest cold. Without roentgenograms, diagnosis may be delayed, since temporary improvement often occurs when the bronchial obstruction is intermittent or when antibiotics are given. There is no distinctive roentgenogram of carcinoma of the lung, however, so any unexplained abnormal roentgenographic findings must be followed up with surgical exploration.

Sixty-two of ninety-one patients with lung cancer were proved cases before autopsy—by biopsy of specimen removed bronchoscopically in thirty-eight, by biopsy of specimen of peripheral or mediastinal lymph nodes or chest wall in eleven, by biopsy of lung specimen at thoracotomy or lobectomy in eight, by cytology of pleural effusion in one, and of sputum and bronchial secretion in four.

All of the patients were men, 62 per cent of whom were less than 50 years of age. Cough was the most common presenting symptom (70 per cent), followed by chest pain and weight loss (55 per cent), and hemoptysis (25 per cent). Physical examination of the chest was negative in twenty-nine patients. Positive findings included various combinations of inspiratory and expiratory sibilant râles, fine to coarse râles, decreased expansion of the involved hemithorax, and dullness over the suspected area. Frequently, a relatively small tumor that occluded a main bronchus gave physical findings suggestive of atelectasis or pneumonia, while a larger lesion peripherally located, if it did not obstruct a main bronchus or invade the pleura, produced few physical signs. It is important to palpate for metastatic peripheral lymph nodes in the axillary, supraclavicular, and cervical regions,

since their involvement indicates inoperability.

Radiation therapy was used in the inoperable patients; it has been of doubtful value. Surgical excision, the only hope of permanent cure, was done in all patients who did not have involvement of the tracheal wall, metastatic lesions to distant nodes and organs, malignant cells in the pleural fluid, or conditions that precluded operative intervention such as severe cardiac or renal disease. In about 50 per cent, resections were palliative, which are considered justifiable because the risk is low and remainder of the patient's life is made more comfortable and is prolonged.

*Forsee, J. H.; Salyer, J. M., and Gants, R. T.: Primary bronchogenic carcinoma. U. S. Armed Forces M. J. 1: 738-749, July, 1950.*

## Resection Justified for Pulmonary Metastasis

A single, malignant metastasis in the lung should be surgically excised when the primary tumor has been completely removed and there is no evidence of further metastatic spread. A study of fifty-two cases in the literature and ten cases at the Mayo Clinic showed that a few patients lived for many years following such a procedure, and that the degree of palliation afforded occasionally justified the attempt.

The primary tumor was a carcinoma twice as often as a sarcoma in the fifty-seven instances in which the type was mentioned. The most common primary sites were carcinoma of the large bowel (eleven), hypernephroma (seven), fibrosarcoma (seven), and carcinoma of the ovary (five). These retained the same rank in the survival group. The time interval between removal of the primary tumor and the appearance of the pulmonary metastasis ranged from zero to forty, but usually was one to four, years. Bronchial involvement was present in 63 per cent of the cases in which it was definitely noted, or 27 per cent of the entire series; the true

percentage probably lies between these two figures, indicating that the tumor will often invade a major bronchus.

The type of operation did not seem to influence survival too greatly, although lobectomy or segmental resection is probably preferable to pneumonectomy when possible. Twenty-three of the sixty-two cases (37 per cent)—thirteen with carcinoma and ten with sarcoma—were living and well at the time when they were reported. The longest survivals were for eighteen and twelve years; two cases were alive and well for six and seven years; and the remainder varied from several months to four years after resection.

Seiler, H. H.; Clagett, O. T., and McDonald, J. R.: Pulmonary resection for metastatic malignant lesions. *J. Thoracic Surg.* 19: 655-675; disc. 675-679, May, 1950.

### Methods and Results with Nitrogen-Mustard Therapy for Lung Cancer

Clinical improvement occurred in 74 per cent of thirty-five patients with inoperable carcinoma of the lung treated with nitrogen mustard (HN2). The improvement usually lasted from two weeks to two months and was evidenced by alleviation of symptoms such as cough, dyspnea, hemoptysis, pain, weakness, and the syndrome associated with superior-vena-cava obstruction; and by such objective changes as regression of pulmonary and metastatic lesions and absorption in pleural effusions. Results were better in the rapidly growing, anaplastic lung cancers than in the more slowly progressing ones.

Always given intravenously, HN2 is most safely administered (in solution) into the tubing of a running intravenous infusion. It should be given in the maximum amount that will not produce serious toxic complications. A single injection of 0.1 mg. of HN2 per Kg. of body weight daily for four days was usually given, but it was subsequently found that some patients were able to tolerate larger doses, particularly those with normal bone marrow. Thus, in

selected cases, total courses of 0.6 to 0.8 mg. per Kg. and single doses of 0.2 and 0.4 mg. per Kg. were given. The authors' current practice is to give 0.2 mg. per Kg. as a single daily dose for two days, a total of 0.4 mg. per Kg. A third injection of 0.2 mg. per Kg. is given if a significant leukopenia has not developed in one week. Ordinarily this completes the course of treatment, but a fourth injection has been given if the therapeutic response was unsatisfactory and if the white-cell count one week after the third dose was not seriously depressed.

The hematological status often did not permit a second course of HN2 upon the recurrence of symptoms. Eight patients received two courses, however; four, three courses; and one, four courses.

In the majority of cases, nausea and vomiting follow each injection within one to eight hours, but these effects usually subside within a few hours. Sedation with barbiturates alleviates the severity of these effects. Pyridoxine is helpful in some patients. Anorexia, weakness, and weight loss commonly occur.

A moderate leukopenia of 2000 to 3000 develops within seven to fourteen days following the usual course of HN2. Excessive dosage produces a toxic syndrome about ten days after treatment, evidenced by severe leukopenia, thrombocytopenia, anemia, fever, and spontaneous hemorrhages in the skin and from various orifices. Blood transfusions and the administration of antibiotics to ward off infection are necessary to avoid a fatal outcome and promote recovery.

Fourteen patients were treated with roentgen rays following HN2, but there was no clear evidence that a more satisfactory or prolonged response or an increased survival time resulted from the combination.

Karnofsky, D. A.; Abelman, W. H.; Craver, L. F., and Burchenal, J. H.: The use of the nitrogen mustards in the palliative treatment of carcinoma. *Cancer* 1: 634-656, Nov., 1948.



## a glance . . .

**one-minute abstracts  
of the current literature  
on cancer . . .**

### **Preventing Swollen Arms Following Radical Mastectomy**

Effective prevention of swollen arms after radical mastectomy was attributed to the use of the Greenough modification of the Rodman incision (in which the incision does not extend onto the arm), drainage for three to five days (serum left in the wound causes fibrosis), avoidance of sepsis, moderate pressure dressings, and, most important, early mobilization of the arm. There was no swelling of the upper arm in forty-one or of the forearm in fifty of ninety patients, in fifty-one of whom the axillary lymph nodes were involved and in one of whom no cancer was found postoperatively. Severe swelling (more than 5 cm.) of the upper arm occurred in only five patients and of the forearm in six, all but two of whom had normal range of motion, though severely disabled by weight.

In the thirteen patients who received prophylactic roentgen-ray therapy following radical mastectomy, recurrences were not prevented, and nine experienced upper-arm swellings of 2.5 to 15.0 cm., and six, swelling of the forearm of 2.5 to 11.0 cm.—those with the greatest amount of swelling being the

ones who had the highest roentgen-ray dosages. The authors recommend postoperative irradiation only after recurrence has ensued.

*Daland, E. M.: The incidence of swollen arms after radical mastectomy and suggestions for prevention. New England J. Med. 242: 497-502, March 30, 1950.*

### **Endometrial Hyperplasia May Mean Theca-Cell Tumor**

Hyperplasia of the endometrium has been found in a considerable number of patients with pre- and postmenopausal bleeding. In such cases, the source of excessive estrogen production should be sought, since it can be attributed to a granulosa or theca-cell tumor in a certain number of patients. Theca-cell tumors accounted for 1.8 per cent of all ovarian tumors during the ten years of review. The ages of the eleven cases ran from 21 to 69 years, with an average of 50 years. Only two of the seven postmenopausal women complained of bleeding; one showed hyperplasia and one, endometrial adenocarcinoma. Two of menopausal, and one premenopausal, women showed bleeding and hyperplasia; one premenopausal had amenorrhea with atrophic endometrium—the menses returned after oper-

ation. Treatment of theca-cell tumors follows the principles of the treatment of ovarian tumors generally—bearing in mind constantly the high malignancy of all ovarian tumors. Radical surgery should be adopted for all bilateral tumors and for unilateral in women 45 years of age or older: resection of the entire uterus, including a small cuff of the vagina, together with both tubes and ovaries.

*Sparling, D. W.: Theca-cell tumors. Am. J. Obst. & Gynec. 59: 1279-1287; disc. 1287-1291, June, 1950.*

### Cervical Carcinoma and Pregnancy

Study of any abnormal bleeding during pregnancy should include inspection of the cervix and biopsy of all definite lesions to rule out cervical carcinoma, since early, immediate treatment means cures to the mothers. In selected cases, the best results are obtained by a combination of radium and roentgen-ray therapy and radical surgery; no patient should be allowed to deliver spontaneously. Of the twelve reported cases, six are living (five after five years), and five children were saved. A high fetal mortality is inevitable (half of these patients were seen before the fetus was viable).

*Johnson, W. O., and Weinfurter, B. J.: Carcinoma of the cervix associated with pregnancy. Am. J. Obst. & Gynec. 59: 1189-1198; disc. 1198-1201, June, 1950.*

### A New Gastroscope for Biopsy

The development of the flexible operating gastroscope in the past two years has made routine gastroscopic biopsy practical in the differential diagnosis of lymphoma, carcinoma, and gastritis. The new model is 2 mm. smaller at the largest diameter, more flexible, and easier to pass than the original model. Sixty-three biopsy specimens have been obtained without accident or complication. In carcinoma of the stomach, a positive gastroscopic biopsy establishes the diagnosis beyond question, but a negative one does not

exclude the lesion because carcinoma may be a localized process and the specimen taken from an uninvolved area.

*Benedict, E. B.: Value of gastric biopsy specimens obtained through the flexible operating gastroscope. Arch. Path. 49: 538-542; disc. 543-544, May, 1950.*

### Treating Testicular Tumors

Unilateral orchiectomy followed by postoperative irradiation with 250 kv. is the treatment of choice in tumors of the testes—more radical surgery or more intensive irradiation not enhancing survival rates. In this series of 216 cases, the five-year-survival rate for seminoma (59.6 per cent) was about twice that for teratoma (24.4 per cent) and four and a half times greater than that for embryonal carcinoma (13.8 per cent). The three forms occurred with about equal frequency. Duration of symptoms and malignancy of the tumor were directly correlated, particularly for seminoma.

*O'Connell, H. V., and Geschickter, C. F.: Tumors of the testes; five-year follow-up study. U.S. Armed Forces M. J. 1: 719-732, July, 1950.*

### Podophyllum Successful in Skin Cancer

Successful results in thirty-three cases show that the resin of podophyllum has a lethal effect on the epithelial tissue of basal-cell epithelioma and the various types of pre-epitheliomatous keratoses. Judgment and experience are necessary in selecting cases, however, for it is not a method to supersede the more conventional ones. The method is simple, practical, and relatively safe—the single exception being damage to the eye if even the slightest trace of the resin touches the cornea. All possible necrotic material is curetted out and removed with gauze, then 20 per cent resin of podophyllum in compound tincture of benzoin is painted on, and a gauze dressing applied (as further insurance against any possible resin being transferred to the eyes). The resin



is reapplied daily, always being preceded by removal of all possible necrotic tissue. Healing is rapid; scarring is less than from electrocoagulation, and the danger of postradiation sequelae is eliminated. Healing time averaged twelve days, ranging from seven to twenty-one days.

Smith, L. M., and Garrett, H. D.: Resin of podophyllum in the treatment of cancerous and precancerous conditions of the skin; effect on basal cell epithelioma and seborrheic, senile and radiation keratoses. *Arch. Dermat. & Syph.* 61: 946-953; disc. 953-956, June, 1950.

### Prevention of Penile Carcinoma

Routine circumcision during infancy should be encouraged as a prophylaxis against penile carcinoma. The evidence is overwhelmingly in favor of the view that the rarity of penile carcinoma among the Jewish people (circumcision on eighth day after birth) and its relative infrequency among Mohammedans (operation between 4 and 8 years of age) is due to their universal practice of circumcision. The operation prevents the accumulation of smegma, which has been demonstrated to be a carcinogenic agent. The absence of smegma may also be the beneficial factor that accounts for the relative infrequency of cervical carcinoma in Jewish women.

Bleich, A. R.: *Prophylaxis of penile carcinoma*. *J.A.M.A.* 143: 1054-1057, July 22, 1950.

### Finding Secondary Heart Tumors

Cardiac signs in a patient with a malignant neoplasm suggest a secondary tumor of the heart, a lesion that is more common than was formerly believed. During a six-year period, secondary tumors of the heart were noted in thirty-eight (8.35 per cent) of all necropsies performed on patients with malignant neoplasms (455). Ninety per cent of these were unsuspected before autopsy. Symptoms are quite variable—they may be absent or appear suddenly as severe heart failure or bizarre arrhythmia. Positive diagnosis can only be made on histological exam-

ination of the myocardium. The primary lesion may be anywhere, but in the majority the breast and bronchus have been the primary sites. Lung involvement is a common finding, regardless of which organ is primarily involved. Pericardial as well as myocardial involvement is frequent.

Dimmette, R. M.: *The ante-mortem diagnosis of secondary tumors of the heart; report of four cases*. *U. S. Armed Forces M. J.* 1: 750-758, July, 1950.

### Signs and Symptoms of Pheochromocytoma

If certain findings (none of which requires unusual facilities) are obtained regularly in the study of hypertensive patients, the diagnosis of pheochromocytoma will rarely be overlooked. Specifically, these are excessive perspiration, peripheral vasoconstriction, and drop in skin temperature during paroxysmal attacks; a normal cold-pressor response; elevations of temperature by 1° F. or more, fasting blood sugar to 120 mg. or more, and basal metabolic rate to plus 20 per cent or more; postural tachycardia; postural hypotension; glycosuria; and paroxysmal attacks of hypertension. Since at least three or four of these signs and symptoms will probably be present, the diagnosis in most cases will be clear enough to warrant surgical exploration. If the condition is recognized before irreversible cardiac damage or sudden death results, recovery after surgical removal is almost invariably dramatic.

Smithwick, R. H.; Greer, W. E. R.; Robertson, C. W., and Wilkins, R. W.: *Pheochromocytoma; a discussion of symptoms, signs and procedures of diagnostic value*. *New England J. Med.* 242: 252-257, Feb. 16, 1950.

### Treatment of Cervical Carcinoma

A report of 200 cases treated from 1934 to 1944 with radium and preliminary deep roentgen rays has been compared with a previous report by the same investigators of 185 cases of carcinoma of the cervix treated by radium alone from 1920 to 1934. In both series,

the percentage of five-year survivors was the same, 37 per cent, indicating that the roentgen-ray therapy was comparatively ineffective in influencing the curability of the carcinoma—although definite clinical advantages were observed. No explanation could be found for a higher percentage of five-year survivals in Stage-I cases, and a lower percentage in Stage-II and Stage-III cases, in the second series.

Wilkins, G. C.: *Carcinoma of the cervix: a report of 200 cases treated with radium and x-rays.* *New England J. Med.* 242: 895-896, June 8, 1950.

### New Syndrome of Diagnostic Significance Described

Melanin spots on the buccal mucosa and lips and polyposis of the small intestine distinguish a syndrome not previously clearly identified. The report is based on twenty-two proved, five probable, and four possible cases—including ten of the authors'. All patients were of dark complexion, although a wide ethnological spread was noted. The syndrome appears to be inherited—however, sporadic cases do occur.

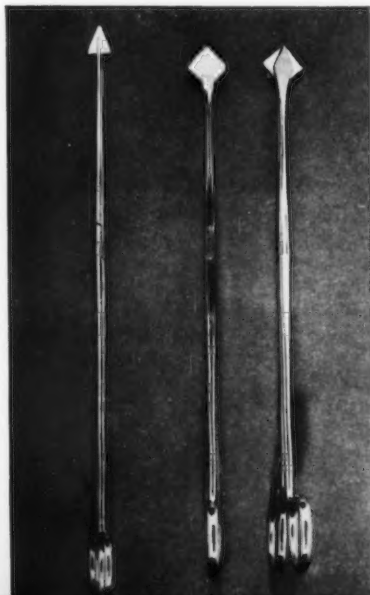
Mouth pigmentation, most prominent on the buccal mucosa, consists of distinctive brown patches (occasionally almost black or blue), 1 to 5 mm. in diameter, which exhibit a stippled appearance under magnification. Small-intestinal symptoms, with absence of large-bowel symptoms, indicate polyps in the small intestine, which involve chiefly the jejunum. The lesions became malignant in three cases and possibly in three others. The face and digits may be pigmented, and the stomach, colon, and rectum may be involved in the polyposis, but the sites of the buccal mucosa and small intestine are the constant features. Both become clinically manifest early in life.

Jeghers, H.; McKusick, V. A., and Katz, K. H.: *Generalized intestinal polyposis and melanin spots of the oral mucosa, lips and digits; a syndrome of diagnostic significance.* *New England J. Med.* 241: 993-1005, Dec. 22; 1031-1036, Dec. 29, 1949.

### Diagnosis with the Sponge Biopsy

The sponge-biopsy method introduced by Gladstone as an adjunct in the diagnosis of uterine carcinoma may make practical the routine survey of unsuspected cases in cancer-detection clinics because of its time-saving simplicity. The cervix is wiped with gauze, and a 1-cm. square of Gelfoam sponge is placed firmly against it for thirty seconds, then rubbed briskly across the surface, and finally placed in 10 per cent formalin and processed. While the specimen does not allow meticulous cytological studies, the slide is simple for the pathologist to read quickly and does not necessitate special training. The results in a study of sixty-eight suspect cases of uterine carcinoma compared favorably with those by the Papanicolaou smear technique and formal biopsy. An alternate method, the use of the sponge instead of absorbent cotton for the Papanicolaou smear to avoid loss of valuable material, suggests the possibility of combining the two techniques.

Rich, J.; Angrist, A. A., and Carpenter, F.: *Gelfoam, vaginal smear, and biopsy in the diagnosis of uterine carcinoma.* *Am. J. Obst. & Gynec.* 59: 1029-1035, May, 1950.



## Helping the Patient with Inoperable and Far-Advanced Carcinoma of the Lung

The patient with inoperable and far-advanced carcinoma of the lung can still be helped. If he will exercise therapeutic perseverance, the physician can contribute toward the maintenance of the patient's activity, comfort, and morale during the inexorable course of the disease. It is true that lung cancer, once it is beyond the curative help of surgery, runs its course within two years in about 90 per cent of the cases, but methods now available for treating these patients with inoperable or far-advanced disease may be expected to provide some degree of palliation and occasionally even to prolong life briefly. For example, when the disease appears to be still confined to a small area, there is evidence (Ariel; Mason)<sup>\*</sup> that carefully directed roentgen-ray therapy will alleviate symptoms and sometimes even retard the progress of the disease temporarily.

Lung cancer tends to spread widely to the lung parenchyma, mediastinal nodes, pericardium, and pleura, and it shows a high frequency of metastases outside the thorax, particularly to the liver, adrenals, kidneys, bone, and brain (Abrams: CA p. 12, November, 1950). Severe symptoms resulting from such extensions of the disease may be temporarily alleviated by roentgen-ray therapy to the site where the disease is causing the disturbance. Thus convulsions due to a cerebral metastasis or severe pain from a bone lesion may be checked.

Nitrogen mustard (HN2) given intravenously has been found in a majority of patients to alleviate partially and temporarily many of the severe pulmonary symptoms (Karnofsky; Lynch).<sup>\*</sup> Unfortunately the therapeutic effects of nitrogen mustard are usually of short duration — from two to eight weeks — and subsequent courses become progressively less effective. In excessive doses, nitrogen mustard also produces severe bone-marrow depression, and each injection is usually attended by

nausea and vomiting. However, despite the hazards of its use and the disagreeable side effects, a trial of nitrogen mustard is justified in patients with extensive disease who have distressing and incapacitating symptoms.

In the anaplastic and oat-cell carcinomas, nitrogen mustard has frequently interrupted the rapid growth of the tumor and temporarily relieved a common complication — compression of the superior vena cava. There is no satisfactory evidence that combining nitrogen mustard and roentgen rays in these cases will result in more effective palliation than either form of treatment alone. In certain cases of widespread disease, however, a course of nitrogen mustard may have a generalized effect, and roentgen rays can then be applied to the disturbing local manifestation. Recently, triethylene melamine, an orally effective agent with nitrogen-mustard-like activity, has been studied in the treatment of lung cancer, and the preliminary results indicate that its therapeutic activity parallels that of nitrogen mustard (Karnofsky).<sup>\*</sup>

Secondary infections, in many cases, may in themselves produce severe pulmonary symptoms, and these can be partially alleviated with appropriate antibiotic therapy. Furthermore, the patient should be supported with blood transfusions, if necessary, proper sedation, and an adequate diet. Oxygen or oxygen-helium, sedatives, and narcotics should be used liberally to relieve pain and discomfort, particularly when more specific attempts at therapy have been exhausted. Active treatment should be continued to the end. In retrospect, it may seem that presently available forms of treatment have not appreciably prolonged life, but the temporary benefit obtained by the patient is always gratifying. Most important of all, perhaps, the continued therapeutic efforts of his physician are proof to the patient that he has not been abandoned.

<sup>\*</sup> Digests of articles by authors referred to will be found in "Keeping up with Cancer," pp. 34-42.

# Role of the Family Doctor in the Cytological Diagnosis of Lung Cancer

*Peter A. Herbut, M.D., and Louis H. Clerf, M.D.*

Because lung cancer yearly accounts for more than 8000 deaths in the United States, is on the increase or is being more frequently recognized than in the past, often masquerades as a viral pneumonia or other pneumonitis, and has a very low over-all cure rate, any procedure that permits earlier diagnosis — particularly a method that can be used by the general practitioner — should receive serious consideration. Such a procedure is the cytological examination of sputum and bronchial secretions; while not the final answer, it does uncover more cases of lung cancer earlier than is otherwise possible and can be used by the one who controls the destiny of the patient — the physician who first sees the case.

## Types of Secretions

Of the three types of material available for cytological examination, we prefer, in the order mentioned, bronchial washings, bronchial secretions, and sputum. However, it is far better to examine sputum than bronchial washings or secretions obtained in a haphazard manner by an inexperienced bronchologist.

*Sputum* is the easiest to obtain and, from the general-practitioner's viewpoint, the most important. It should be properly collected and examined in every case in which carcinoma of the lung is suspected. One should not, however, wait for sputum to appear because, only too frequently, by the time material is expectorated the disease is already incurable. Also, only a positive report should be considered significant. A negative report, or even repeated negative reports, mean nothing — are not proof that the patient is free of cancer.

*Bronchial secretions* are usually obtained only at the time of bronchoscopic examination and necessitate sending the patient to a physician specifically qualified in this field. Bronchoscopic studies, in our opinion, should always be done when sputum is negative or not present. At the time of bronchoscopic examination, *bronchial washings* are also obtained from the segment of the lung containing the suspected tumor.

## Methods of Collection

*Sputum* is obtained by having the patient cough into a clean receptacle. One should make sure that the material expectorated comes from the depth of the chest rather than from the nasopharynx. The material expectorated the first thing in the morning is frequently sufficient, although sometimes a twelve- or twenty-four-hour specimen is desirable. In the latter instance, the receptacle should contain several ounces of 95 per cent alcohol as a preservative. If only a single morning specimen is used, a preservative is not necessary provided the specimen reaches the laboratory within an hour after expectoration.

*Bronchial secretions* and washings are collected, as already stated, with the aid of a bronchoscope. A careful physical examination and a roentgenogram of the chest — to localize the site of the new growth — are mandatory prior to bronchoscopic examination. Secretions that may be present in the trachea and the main bronchi are either by-passed if they are

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*From the Departments of Pathology and Broncho-esophagology, Jefferson Medical College and Hospital, Philadelphia, Pa.*

scanty, or aspirated and preserved for cytological examination, or discarded.

### Gross Appearance of Secretions

Neither the gross appearance, the quantity, nor the consistency of sputum, bronchial secretions, or bronchial washings discloses anything of diagnostic importance. Tenacious, hemorrhagic, or dark-brown material may be obtained from patients with many types of inflammatory diseases, and, conversely, material completely free of blood may be loaded with neoplastic cells.

### Preparation and Staining of Smears

The ideal setup is to have a laboratory handy where the freshly collected material may be examined without delay. In the laboratory the sputum, bronchial secretions, or bronchial washings are poured in a Petri dish and examined over a black background. When present, the grossly bloody portions or small granules that may represent pieces of tissue are fished out with wooden applicators and put upon three ordinary, clean, new glass slides. Thin smears are prepared by covering each slide with an additional slide and compressing the material deposited. When the ultimate thickness of the film of specimen is no greater than that of an ordinary blood smear, the slides are pulled apart and dropped immediately in a Coplin jar containing a mixture of equal parts of 95 per cent alcohol and ether. After fixing from ten to twenty minutes, the slides are stained by the Papanicolaou technique or any other usual method.

If a laboratory is not available, the material collected is fixed in 95 per cent alcohol (at least two volumes of alcohol to one volume of material) and mailed to the laboratory. While this procedure is carried out successfully in some centers, we prefer to have slides prepared immediately after the specimen is obtained, fixed in equal parts of 95 per cent alcohol and ether, removed, allowed to dry at room temperature, and sent by mail in the unstained state.

### Microscopic Interpretation

In the microscopic interpretation of the smears, the cytologist looks for the usual

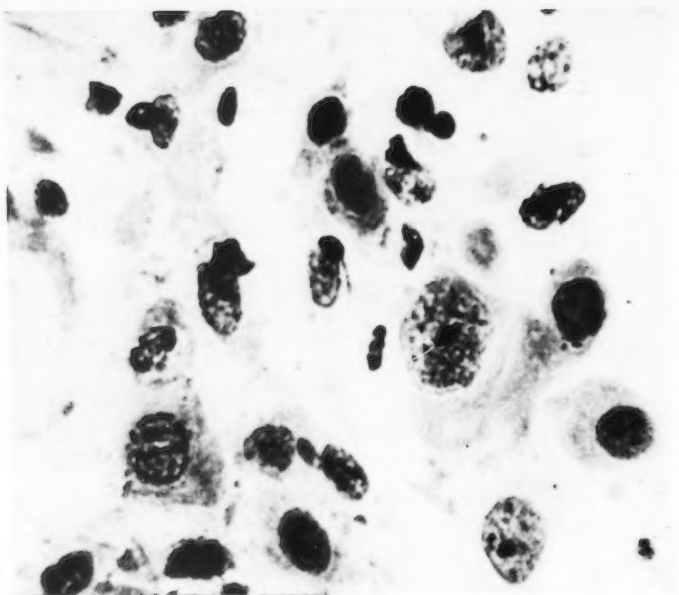
characteristics of variations in shape, size, and staining qualities of cancerous cells as compared with normal epithelium. The details of this are not important to the general practitioner. It cannot be over-emphasized, however, that recognition of neoplastic cells, while easy for the well-trained person, is difficult and even impossible for the novice. Unless a pathologist has made a special effort to become acquainted with the appearance of normal and abnormal epithelial cells in sputum, bronchial secretions, or bronchial washings, and unless he has a constant and adequate flow of material through his office, he cannot be expected to evaluate the smears properly. There are numerous centers throughout the United States to which such preparations can be sent for precise evaluation. Such centers, thanks in part to the American Cancer Society, are constantly increasing in number.

### Results

In well-organized clinics, a correct positive cytological diagnosis of carcinoma of the lung is being made at present in from 70 to 95 per cent of all cases of cancer of the lung seen. Our own figures, which consist almost solely of examination of bronchial secretions and bronchial washings, are as follows: In a consecutive series of 379 proved cases of carcinoma of the lung, neoplastic cells were present in the secretions in 331, or 87 per cent; bronchoscopic biopsy was possible in 124 patients, or 33 per cent; stenosis, fixation, displacement, etc., of the bronchus (without positive biopsy) were present in 113 cases; neoplastic cells were present in secretions and bronchoscopic examination was completely negative in 113 cases, or 30 per cent.

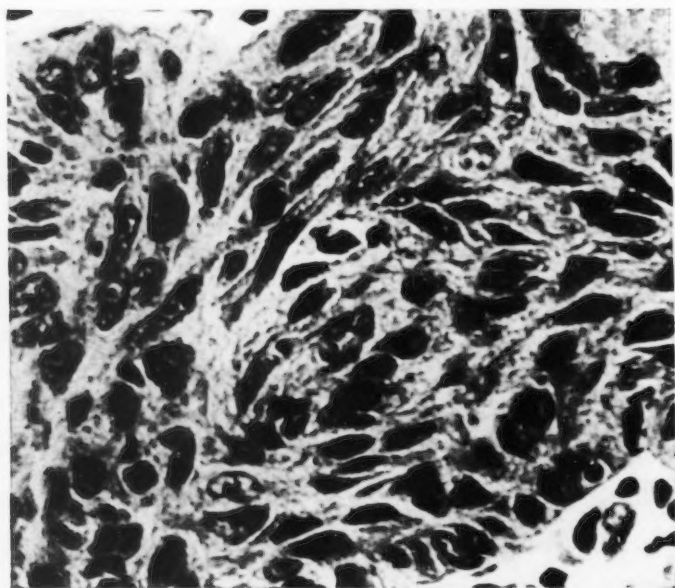
### Conclusions

From the viewpoint of the general practitioner, it can be safely stated that for every patient suspected of having carcinoma of the lung: (1) he should have an examination of sputum, bronchial secretion, or bronchial washings; (2) the smears should be interpreted by a competent, especially trained cytologist; and (3) a positive report only can be considered conclusive — a negative report does not mean that the patient is free of cancer.

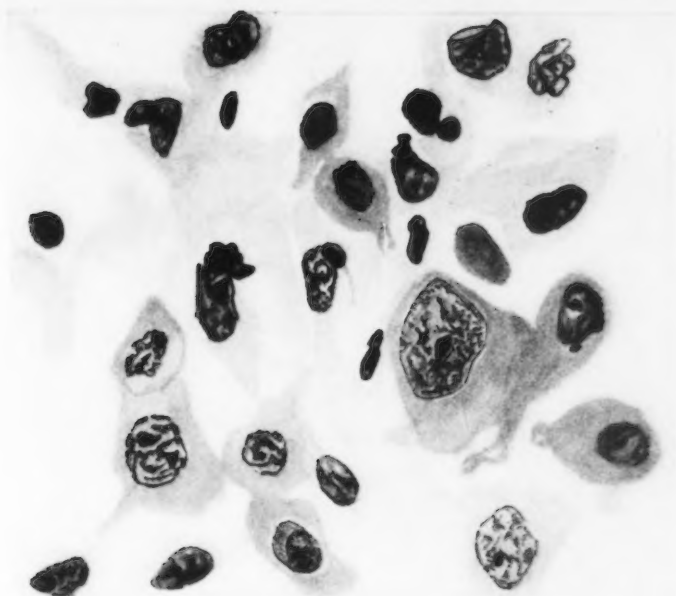


Field of nuclei with and without cytoplasm, showing great variation in size and shape.

Histological section: squamous-cell carcinoma of the lung.







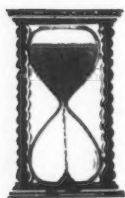
#### KEY TO SQUAMOUS-CELL CARCINOMA IN SPUTUM

- 1 Differentiated malignant cell with irregular strands of chromatin and prominent nucleolus.
- 2 Irregular malignant nucleus, well-defined cytoplasmic cell border.
- 3 Elongated undifferentiated malignant cell without cellular borders.
- 4 Wrinkled undifferentiated nucleus with strands of chromatin, indistinct cytoplasm.
- 5 Large irregular differentiated cell with abnormal chromatin pattern and large nucleolus.
- 6 Nucleus with irregular nuclear pattern but no distinct chromatin. The field is filled with many other differentiated and undifferentiated malignant cells varying in size and shape.

Illustrations on pages 50 and 51 are from "The Cytologic Diagnosis of Cancer," reprinted by courtesy of the Vincent Memorial Hospital and W. B. Saunders Company, Philadelphia.

## THE PROGRESSION OF LUNG CANCER

The roentgenograms on these four pages depict cancer of the lung through four phases of growth. These stages have no clear-cut boundaries nor do they represent any sort of dogmatic classification.



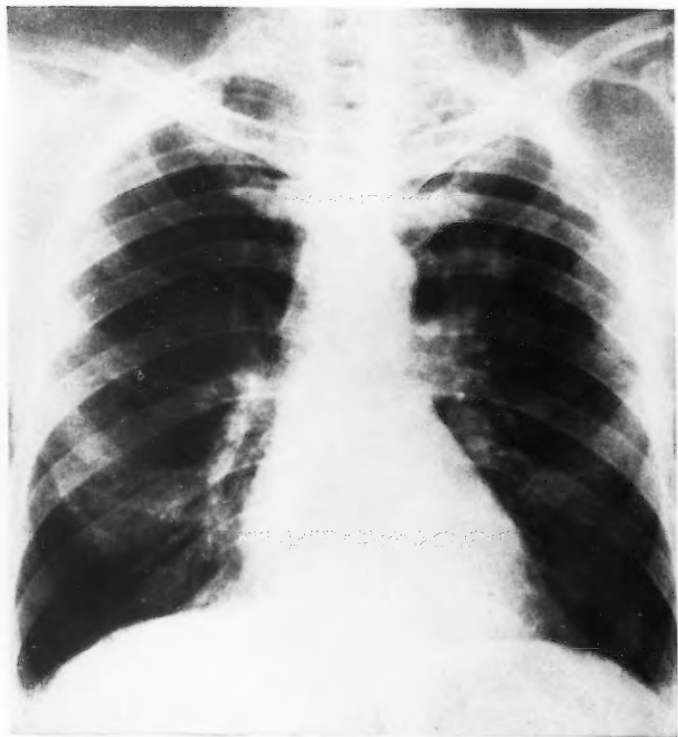
**THE LATENT PHASE** — This encompasses the period from the first abnormal cell until the colony of cancer cells has grown out of microscopic size. *Not discoverable.*

**Figure 1** This 45-year-old physician had had a carcinophobia for several years. He was frequently examined. This roentgenogram was properly read: "No pulmonary pathology of present clinical significance." Note the several healed tubercles. Subsequent events showed that even at this time he probably had cancer of the left upper lobe.



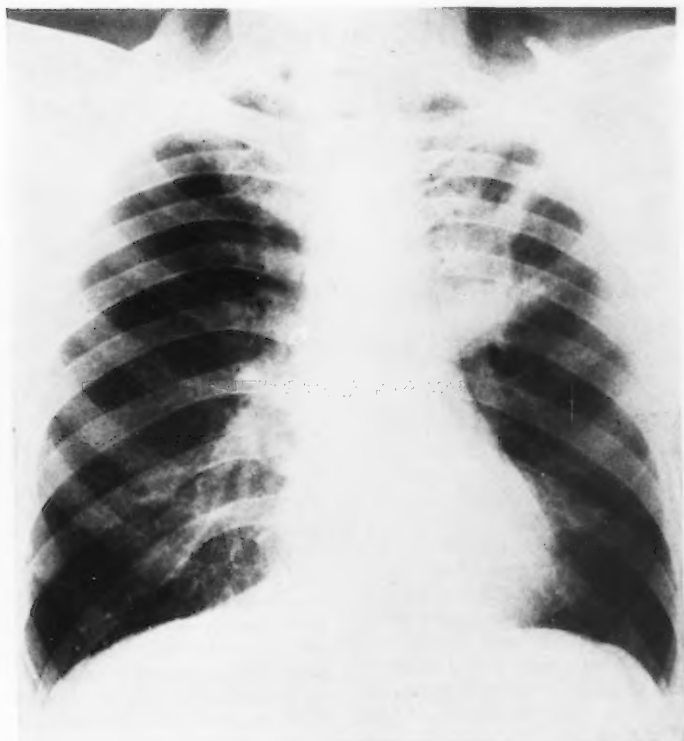
**THE SILENT PHASE** — This is the period peculiar to many lung tumors in which they are potentially manifest (abnormal shadow on screening film) but have not as yet caused symptoms. *Usually curable.*

**Figure 2** Six months later, this roentgenogram showed abnormality in the second interspace on the left. Since the patient was clinically well, he was not told of this defect, and it was read as insignificant.



**THE URGENT PHASE** — This is the period in which the tumor urges attention by means of such symptoms as persistent cough, chest discomfort, wheezing, hemoptysis, or by recurrent or protracted febrile reactions, resulting from secondary pyogenic or virus infections. *Sometimes curable.*

**Figure 3** Four months later, the physician had a hemoptysis. The film showed slight increase in the left upper-lobe abnormality. In spite of the patient's apprehension of cancer, he was persuaded that he had pneumonia. Although the lesion failed to respond to antibiotic therapy, the misdiagnosis was carried for another four months.



**THE RAMPANT PHASE**—This is the period in which the growth is invading areas outside the lung. Clinical evidence of cancer is then obvious. *Incurable.*

**Figure 4** Four months later, the roentgenogram showed progressive increase. The patient was sent to a thoracic surgeon. Bronchoscopic examination and biopsy of cervical nodes showed an incurable cancer, primary in the lung and with widespread metastases.

## DOCTORS DILEMMAS

**Q** *Actually, what basis is there for optimism concerning the five-year survival of patients with gastric cancer?*

**A** When we recall that the resectability rate of patients with gastric cancer was approximately 2.9 per cent during the years between 1916 and 1930, and rose to 39.8 per cent for the five-year period between 1942 and 1946, it becomes apparent that earlier diagnosis, refinements in technique, and improvements in pre- and post-operative management have tremendously increased the number of patients with resectable gastric cancer.

A recently reported series shows that 35 per cent of patients with resectable gastric cancer may be expected to live five years or longer. This is impressive evidence that earlier diagnosis and aggressive treatment may properly be expected to result in appreciable improvement of the five-year-survival rate for patients with gastric cancer.

**Q** *An increasing number of elderly patients are seeking advice concerning treatment of keratoses on their faces and hands. Should these invariably be removed?*

**A** Many lesions of the skin, per se benign, have eventuated into cancer. Not infrequently, the so-called senile keratoses become squamous-cell cancer, and therefore they should be treated promptly. Freezing with solid carbon dioxide, electrodesiccation, and curettage, or appropriate roentgen-ray

therapy will give satisfactory results. It is imperative, however, that where there is the slightest suspicion that cancer may be present, the entire lesion should be widely excised and the specimen submitted for microscopic examination.

**Q** *What is the prognosis in cancer of the larynx?*

**A** The prognosis is influenced by a number of factors, especially the size of the growth and the presence or absence of cervical metastases. The importance of these factors can be plainly shown by the fact that if the tumor on the vocal cord measures 1 cm. or less in diameter, a five-year cure rate of 95 per cent may be obtained by partial laryngectomy or laryngofissure. The cure rate in larger lesions of the intrinsic larynx and in any lesion of the extrinsic larynx is definitely lower.

**Q** *Is there any biologic test today that is sufficiently reliable to be used as a diagnostic test for cancer?*

**A** No. The overenthusiasm and optimism of the lay press for several cautious announcements in the recent medical literature have not been justified by reports of responsible investigators themselves. Findings, however, have been provocative, and it is probably not unreasonable to anticipate refinement of some such acceptable procedure as an aid in the diagnosis of cancer.



**Q** A "lump" or nodule has recently been discovered by a woman, aged 24, in the mid-line of her neck anteriorly. It now measures about 2 cm. in diameter. Is it safe to watch this "lump," advising removal only if it increases in size or gives any symptoms, which it does not at present?

**A** A nodule in the thyroid should not be merely "watched" for further enlargement or development of symptoms any more than should a lump in the breast. It is true that about 90 per cent of such thyroid nodules are adenomas only, but approximately 10 per cent prove to be carcinoma. Often these tumors are found to be malignant by microscopic examination only. A single, solitary adenoma is more apt to contain cancer than are multiple adenomas. It also may be true that cancer in adenomas occurs more frequently in men than in women.

**Q** What should be done for an area of leukoplakia on the buccal mucosa near the gingivobuccal gutter?

**A** A biopsy should be taken. If it shows leukoplakia only, the lesion must still be considered a precancerous lesion and should be completely excised. If the patient is addicted to smoking, the habit should be broken at once. Particular attention must be paid to dental hygiene and ill-fitting dentures. The association of the development of leukoplakia with vitamin-B deficiency has not been proved, but some patients

have shown marked improvement with large doses of vitamin-B complex. This medication should be given daily, intramuscularly, since the drug is not utilized by intraoral administration if a real vitamin-B insufficiency has developed, but when given intramuscularly is readily picked up by the circulation.

**Q** Should Wilms's tumor in children be given preoperative irradiation?

**A** This procedure is followed by some experienced physicians. The tumor may be radioresistant, however, and it is usually preferable to operate as early as possible after a provisional diagnosis has been made.

**Q** Recent radio and newspaper references to leukemia in children seem to indicate that the disease is increasing in frequency and that new developments in treatment offer these children appreciable palliation. Is this actually so?

**A** It cannot be said that leukemia itself is occurring with greater frequency, but it is certainly true that leukemia and many other neoplastic diseases are being recognized with greater frequency than heretofore. Of the newer treatments, the folic acid antagonists have been effective in securing appreciable prolongation of comfortable life in approximately 30 per cent of children with acute leukemia.

# CANCER CLINICS



The patient, M. H. (No. 174757), an unmarried 16-year-old Negress, a cotton picker, entered the Barnes Hospital, July 31, 1949. She was too ill to give her history, and the data available were scanty. Her chief complaint was said to be fever, drowsiness, left chest pain, and a skin eruption. The family history, past history, and systemic review were noncontributory. One month before admission, she developed a sore throat, swollen cervical glands, and a sensation of tightness in the chest. Her physician made a diagnosis of tonsillitis. He gave her a green liquid medicine, and her complaints apparently disappeared in a few days; she continued, however, to take the medicine until admission.

After a few days, during which she was asymptomatic, she again developed a mild sore throat; about two weeks before admission, weakness and malaise appeared, and she was forced to take to her bed. She developed an eruption, first over the face, then over the neck and trunk, which was de-

scribed as "red, tiny, grain-like lumps." There was no itching, but some of the nodules were tender. New lesions appeared from time to time and some older ones regressed.

A week before entry, pain developed in the left lower chest associated with a nonproductive cough. She was given penicillin daily. During this week, her appetite failed, she complained of feverishness, and had several chills. Her drowsiness increased and she was out of contact with her surroundings most of the time. There was no history of either gastrointestinal- or genitourinary-tract symptoms and no known exposure to either tuberculosis or syphilis; a blood test was said to have been negative.

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Condensed from Skin Eruption, Obtundity and Pyrexia. *Am. J. Med.* 8:384-392, 1950. Published by permission of the Department of Medicine, Washington University School of Medicine and the Barnes Hospital, and The American Journal of Medicine.

On admission, the patient had a temperature of 41° C., pulse 160, respirations 65, and blood pressure 120/70. The patient was a well-developed young colored woman who appeared acutely ill and somewhat obtunded. The skin was dry. There were many raised, hard, red papules over the face, neck, and trunk, but only occasional ones on the extremities; they varied from 0.2 to 1.2 cm. in diameter and appeared to be of varying duration. (Figure 1.) Some had exfoliated and were deeply pigmented. The lesions were not vesicular; they seemed to involve both the skin and the subcutaneous tissue. There was generalized lymphadenopathy; the nodes, 1 to 2 cm. in diameter, were firm but not tender. Several conjunctival lesions not unlike those on the skin were described, and in the left lower conjunctival sac

Figure 1. Gross appearance of the skin lesions.



there was a lesion that resembled a mucous patch. The pupils reacted normally to light and accommodation and the fundi appeared normal. The nasal mucosa was crusted and dry and several small bleeding points were seen. The lips were dry and covered with a scaling crust. The tonsils were definitely enlarged. The neck was somewhat stiff to anterior flexion. Respirations were rapid and shallow. There was dullness to percussion over the left posterior lung field and lower axilla, and over this area, the breath sounds were diminished and a few moist râles were heard. Examination of the heart revealed the maximum apical impulse to be in the left fifth interspace, 6 cm. from the mid-sternal line. There was a diffuse rippling pulsation over the entire precordium. The rhythm was regular and the first apical sound was split. No murmurs were heard. Palpation of the abdomen was unsatisfactory, but there was some tenderness in the epigastrium and in the right upper quadrant. The liver was felt 6 cm. below the costal margin but the spleen was not palpable. Pelvic and rectal examinations were negative. Neurological examination revealed hypoaactive reflexes.

The laboratory findings were as follows: blood count: red cells, 3,510,000; hemoglobin, 9.5 gm.; white cells, 25,150; differential count: juvenile forms, 4 per cent; stab forms, 22 per cent; segmented forms, 64 per cent; lymphocytes, 20 per cent. Very few platelets were seen and there were two normoblasts per 100 white cells. Urinalysis and urine culture, negative; stool examination, guaiac negative; blood Kahn test, negative; blood cultures, negative (and remained so). Blood chemistry: non-protein nitrogen, 19 mg. per cent; total protein, 5.8 gm. per cent; albumin, 3.5 gm. per cent;

globulin, 2.3 gm. per cent. Agglutinations versus typhoid, paratyphoid, brucella, and tularensis antigens were negative; cold agglutinin test, negative. Stool culture: no pathogenic organisms were isolated. Sputum smear: no acid-fast bacilli. Sputum culture: *Staphylococcus albus*, nonhemolytic streptococcus. Electrocardiogram: normal. Roentgenograms of the chest showed an increase in lung markings bilaterally with small, fine, nodular areas of density in both lung fields interpreted as bilateral bronchopneumonia. A flat roentgenogram of the abdomen showed marked hepatosplenomegaly. The spinal fluid was normal.

The patient was given intravenous fluids, oxygen by nasal catheter, and adequate doses of penicillin, streptomycin, and aureomycin. In the first twenty-four hours after admission, there was little change in her condition. On the second day she had a chill and her temperature spiked from 39.5° to 41° C. The signs at the left base remained unchanged. On the third day, her temperature had fallen to 37.4° C. Coccidioidin, histoplasmin, the first strength P.P.D. skin tests were negative.

A dermatologist described the skin lesions as extraordinary in appearance and suggested the possibility of bromide intoxication. Blood bromides were above normal, but the green liquid medicine had contained bromide. Blood chlorides and carbon dioxide combining power were normal. Liver function was disturbed.

A sternal-marrow aspiration showed stimulation of the myeloid cells, some shift to the left, and an increase in mitotic figures. Many myelocytes showed vacuolization and toxic granules. Plasmodia, *Histoplasma*, *Toxoplasma*, and tubercle bacilli could not be found. Another chest roentgenogram showed fluid in the right pleural cavity; the infiltration at the right base had progressed and there was thickening of the minor lobar fissure on that side. The

diagnosis was now: bilateral bronchopneumonia, right pleural effusion, and pleurisy.

In spite of treatment, the temperature rose, respirations were 40 to 60 a minute during the last three days of life.

### Clinical Discussion

Dr. Harry L. Alexander: When this patient was admitted, she presented a very difficult diagnostic problem and we face the same problem today. It was first thought by the house staff that she had an acute fulminating infection. After brominism was suggested as the cause of the skin eruption, the situation was, if anything, even more difficult to evaluate. Dr. Hunter, had you seen this patient with the information which we have at hand now, what diagnosis would have seemed most probable to you?

Dr. Thomas H. Hunter: Whenever one sees a young Negress who is acutely ill with a disease that involves the lungs, he should consider tuberculosis. I think that disseminated tuberculosis must certainly be considered as one of the most likely probabilities. Hepatomegaly and splenomegaly are consistent with it, although the leukocytosis of 25,000 with a marked left shift would be somewhat unusual. She exhibited some evidence of central-nervous-system involvement; and before one knew the results of the lumbar puncture, he might also have seriously considered tuberculous meningitis.

Dr. Alfred Goldman: Generalized lymphadenopathy is entirely consistent with a diagnosis of tuberculosis.

Dr. Hunter: Could the generalized involvement of lymph nodes have resulted from the skin eruption?

Dr. Richard S. Weiss: If the skin lesions had been the site of a secondary pyogenic infection, I would not have been surprised to find generalized lymphadenopathy. Otherwise, I would think it would be unusual.

Dr. Edward H. Reinhard: I saw this

patient just before she died. Many of the skin nodules were of considerable size. Are discrete nodules common in bromide eruptions?

Dr. Weiss: Bromide eruptions are rather peculiar and often appear in one of two forms: first, as an erythematous lesion such as erythema multiforme with urticarial phenomena and, second, as nodular granulomas such as were seen in this patient. Her lesions were discrete and many of them were keratotic on their uppermost surface. In some areas they were verrucous. Some appeared to be involuting, and in a number of areas, there were pigmented spots that we interpreted as sites of completely involuted lesions. When we saw the patient, we were unable to associate the skin lesions with anything other than a bromide eruption. They were not at all like the nodular tuberculids that one sees in disseminated tuberculosis; for example, the centers of this girl's lesions were not necrotic and did not slough out. Also, the fact that she was somewhat obtunded seemed entirely compatible with the diagnosis of bromide intoxication. However, patients who show the systemic manifestations of bromide intoxication rarely, if ever, develop bromide eruptions.

Dr. Alexander: Does the negative first strength P.P.D. skin test rule out tuberculosis?

Dr. Carl G. Harford: No, it does not.

Dr. Alexander: Dr. Grunow, do you think the findings on the chest roentgenogram are suggestive of tuberculosis?

Dr. Otto H. W. Grunow: I should say the findings are definitely not suggestive of tuberculosis, Dr. Alexander.

Student: May we ask Dr. Goldman if this patient could not possibly have had the primary type of tuberculosis?

Dr. Goldman: If indeed she had tuberculosis, that is probably the form in which it existed; but I doubt seriously if tuberculosis is the correct diagnosis. Histoplasmosis might have pro-

duced a clinical picture such as this patient exhibited.

Dr. Alexander: Your point is well taken. Certainly the combination of hepatomegaly, splenomegaly, fever, and pulmonary infiltration suggests histoplasmosis. The bone marrow was studied very carefully, however, and no organisms were found.

Dr. Alexander: Are there any other suggestions?

Dr. Harford: Along with Dr. Goldman's suggestion of histoplasmosis, I should like to bring up for consideration the diagnosis of systemic blastomycosis. This disease is also rare, but it characteristically produces pulmonary findings, subcutaneous nodules, a leukocytosis with a left shift, and one would not expect it to respond especially well to antibiotics.

Dr. Alexander: Certainly blastomycosis should be considered, Dr. Harford.

Dr. Albert I. Mendeloff: Can Dr. Reinhard assure us that this patient did not have acute Hodgkin's disease? She had a large liver and spleen and an acute fulminating course. Does the single bone-marrow examination and the multiple peripheral-blood examinations rule out that diagnosis?

Dr. Reinhard: When I saw this patient the diagnosis of Hodgkin's disease did not suggest itself to me. However, there is nothing in the history or course that is incompatible with it.

Dr. Hunter: Could she have had fulminating atypical pneumonia? Peculiar neurological symptoms may occur in such patients when they are extremely ill, and one important finding was the marked tachypnea that continued throughout her course. Had she had atypical pneumonia she probably should have responded to the large doses of aureomycin she received, although the value of aureomycin in atypical pneumonia is not yet proved. A leukocyte count of 25,000 is somewhat uncommon in atypical pneumonia but may occur.

Dr. Alexander: The negative cold agglutinins are somewhat against that diagnosis, Dr. Hunter.

Dr. Hunter: Yes, although they are positive in only 75 per cent of cases. I don't think that primary atypical pneumonia is a likely diagnosis, but have suggested it because this situation is so complicated.

Dr. Alexander: One suggestion that was made during the patient's course in the hospital was tularemia. Dr. Wood, would you be surprised if this patient did have tularemia?

Dr. Wood: It is possible that this patient originally had tularemic tonsillitis and subsequent systemic spread. I have never observed a skin eruption in tularemia, but this can be explained by the bromidism. The course of the disease was rather long for tularemia, however, and the patient should have responded to antibiotic therapy. Finally, the negative tularensis agglutination militates against the diagnosis of tularemia.

Dr. Edward Massie: May I suggest as a further possibility acute bacterial endocarditis, which should be considered as one of the causes of fever of unknown origin.

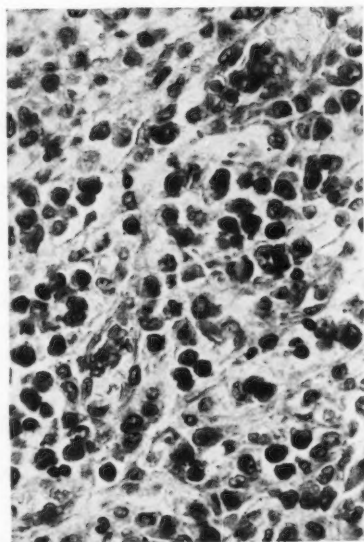
Dr. Alexander: Now, for purposes of discussion, the fact that a skin biopsy was obtained before the patient died was not included in the case history. I shall ask Dr. Moore to tell us about the results of the biopsy.

Dr. Robert A. Moore: Dr. Ackerman examined the skin biopsy and made a diagnosis of reticulum-cell sarcoma. Figure 2 shows the cell type found within the nodule. It is a relatively large cell with eosinophilic, moderately dense cytoplasm, a fairly large nucleus, and a nucleolus. All of us who saw this slide subsequently concurred in the diagnosis of reticulum-cell sarcoma. At autopsy, this essential type of tumor cell was found throughout the body. The histological changes indicated a neoplastic disease of cells derived from the reticulo-endothelial system.

Dr. Alexander: The diagnosis of reticulum-cell sarcoma was certainly not suggested before the results of the biopsy were made known. I should like to congratulate Dr. Mendeloff whose suggestion of Hodgkin's disease closely approached the correct diagnosis. It is quite clear now that none of the therapeutic measures employed could have changed the course of this patient's illness, and nitrogen-mustard therapy was not used because she was moribund before the correct diagnosis was known.

*Final Anatomical Diagnoses:* Malignant lymphoma, reticulum-cell type, involving lymph nodes, liver, spleen, lungs, pleura, skin, mucosa of the esophagus and stomach, lymphoid follicles of the colon and bone marrow; fatty degeneration of the myocardium; microscopic fragmentation of the myocardial fibers; bilateral hydrothorax; congestion and edema of the lungs.

Figure 2. Reticulum-cell type was the infiltrating cell in all the lesions. This section is from a lymph node; but, except for a variable degree of fibrosis, the lesions in all sites were similar.







1



2



3



4

## PIONEERS IN SURGERY OF THE LUNG

An operation by Ratjen, in the earlier 1800's, showed that man could live for some time after unilateral pneumonectomy. The operation met with condemnation, however: "The first, woeful success in man should have cooled even the most enthusiastic spirits."

- 1 In 1883, Rudolf Krönlein, Zurich, operated successfully on an 18-year-old girl and removed not only a part of the pleura but also a part of the lung.
- 2 In 1888, H. Roswell Park, of Buffalo, removed a large portion of the chest wall and excised the lung mass involved by a spindle-cell sarcoma. The patient lived for six days.
- 3 In 1908, Ferdinand Sauerbruch, Berlin, excised the left lower lobe of the lung for carcinoma, using a differential-pressure apparatus. The patient was discharged six weeks later.
- 4 In 1933, Evarts Graham, St. Louis, removed the entire left lung for bronchogenic carcinoma, the first time this operation had been performed upon a human. The patient, a physician, is still in active practice.







# new developments in cancer

## Diet and Cancer...

In fruit flies, diet seems to play a role in the development of cancer.

Dr. L. P. Wilson of Wellesley has a strain of *Drosophila* that almost always develops melanoma. The "black cancer" shortens life of the fruit fly a little, and curtails the number of eggs a lot.

Longevity and freedom from cancer in these fruit flies are inversely proportional to the amount of food they eat. The overfed die early; the underfed live long and frequently do not develop melanoma. The vitamin content of the food doesn't make much difference one way or another.

## Beryllium...

Beryllium, that scarce and highly toxic metal used in roentgen-ray apparatus, fluorescent lamps, and radio tubes, is also turning out to be of interest in cancer research.

The development of skin cancers among people who came in contact with beryllium in the fluorescent-light industry has aroused scientific curiosity at Massachusetts General Hospital. Research there is concerned with its carcinogenic qualities.

University of Cincinnati scientists

have found that when beryllium oxide is injected intravenously into rabbits it concentrates in the liver, spleen, lung, and other tissues and causes lethal bone tumors, which metastasize to the lung.

At Kenyon College an investigator has found that beryllium can stop at least one kind of growth. When beryllium nitrate is injected into salamanders whose limbs have been amputated, the chemical concentrates on the wound surface and there is no regeneration of the limb. When the limb again is severed a tenth of a centimeter higher, it regenerates completely. Apparently the beryllium compound has collected completely on the wound surface and has inhibited growth there.

## Normal Tissue Outgrows Cancer...

Dr. S. Meryl Rose at Smith College has shown that normal regenerating tissue in one instance outgrows—and reforms—cancer in salamanders.

The scientist transplants frog-kidney cancer to the limbs of salamanders where it thrives. When the limbs are amputated just below the transplant, not only do limbs regenerate but, in the process, the new growth transforms malignant to normal tissue.

### **Two Heads — No Tails . . .**

State University of Iowa scientists are working on one of the oddest phenomena of growth. At will they can cause a flatworm to grow a tail where the head should be.

Drs. Gordon Marsh and H. W. Beams found a few years ago that when they passed a direct current through a regenerating flatworm, the head formed on the end nearest the cathode and the tail on the end nearest the anode. The electrical potential had to be kept constant. When the tail was cut off and the amputated surface turned toward the cathode, a second head developed where the tail once was.

They have not been able to develop a headless, two-tailed worm but they have been able to arrest the growth of the head by turning the decapitated end toward the anode.

Does polarity have anything to do with the growth of cancer? Or with the growth of normal tissues in humans? That's the big question in this laboratory.

### **In Vitro Fertilization . . .**

Life, meant to begin in the warmth and darkness of the womb, has been started in the bright light of the laboratory.

Scientists at the Free Hospital for Women in Boston have succeeded in fertilizing human ova in watch glasses containing human sperm. So far the embryos have not developed beyond a few cells, but they are shedding some light on the chemical and physical mechanisms of early growth.

### **Fast and Slow Cancers . . .**

There have been records of cancers that, untreated, grew for as long as thirty-five years without killing the patient.

Other cancers, seemingly nipped in the bud, have snuffed out life within a few months. And there have been cases—one in 80,000, an authority estimated—that regressed spontaneously and completely.

Scientists at the University of Oklahoma School of Medicine have been exploring the reticulo-endothelial system for answers to the rate of tumor growth. They have been trying to determine whether resistance to cancer could be related to the mechanism that produced antibodies. Measurements of the disappearance of colloidal dyes from the blood stream may provide a yardstick of the individual's ability to combat foreign proteins.

### **The Chemistry of Cancer . . .**

Some of the answers to the chemistry of a few cancers have been turned up at Washington University, St. Louis.

Scientists there have found that epithelial cells lose as much as 50 or 60 per cent of their calcium and iron during precancerous stages of carcinogenesis. More is lost as cancer develops. Also dissipated in the process were zinc and copper. Little affected, if at all, were sodium, potassium, and magnesium.

### **Mutagens and Carcinogens . . .**

Stanford scientists have found that at least seven carcinogenic rays and chemicals are mutagens as well.

Using mold cultures of *Neurospora* as a testing ground, Drs. Edward L. Tatum and Raymond W. Barratt stepped up mutation rates four times normal with some carcinogens and two hundred times normal with others. Roentgen-rays and nitrogen mustards were powerful mutagens.

Now the scientists are testing mutagenic capacities of chemicals that, so

far, have failed to produce cancers but are structurally related to carcinogenic hydrocarbons.

### Heat Measurements . . .

Yale scientists have built a heat-measuring device so sensitive that a tiny spark registers like a holocaust.

The microcalorimeter will show temperature changes as slight as ten millionths of a degree Fahrenheit. It shows how much heat is given off in such chemical reactions as the breaking up of proteins by enzymes, immunological activity between antigens and antibodies, or the change in activity of enzymes in alkaline or acid environment.

### Postfellowship Research Grants . . .

Five awards of \$18,000 each will be granted by the American Cancer Society to promising young scientists who have finished their fellowship training. Mefford R. Runyon, Executive Vice-President of the American Cancer Society, said that the purpose of the program is to retain highly competent young scientists in cancer research by helping them over the first few years of "plodding, obscurity and unremunerative work." The institutions will receive the payments over a period of three years to be applied to the scientist's support, research, or both.

### N.R.C. Names Dr. Wason . . .

Dr. Isabel M. Wason, Professional Assistant to the Subcommittee on Oncology, National Research Council, has assumed duties as the Executive Secretary of the new N.R.C. Committee on Cancer Diagnosis and Therapy, which is being set up for the purpose of facilitating the work of existing organizations. A graduate of Johns Hopkins

Medical School, Dr. Wason was with the Department of Pathology and Bacteriology at Yale University School of Medicine for seven years, leaving in 1925 as Assistant Professor. Until Sept. 1, 1949, she served as Pathologist and Director of the Laboratory at St. Luke's Hospital, New Bedford, Mass., where for more than fifteen years she was also on the local committee for the State-supported Cancer Clinic.

### Rees-Evans "Cancer Cure" . . .

The publicity given the Rees-Evans "secret remedy" for cancer by the London *Picture Post* was called "distinctly premature" and "unfortunate" in a statement issued by the Presbyterian Hospital, Newark, N. J., where the "remedy" had been studied. In view of the limited number of cases and the short period of time elapsed since therapy was initiated, it is considered that the results are inconclusive. In an editorial on the subject, the *British Medical Journal* points out the lack of evidence for the statements made in the *Picture Post* and calls this publicity "dangerous nonsense." It is said that no one but Mr. Rees-Evans knows what this "secret remedy" is, and that he refused to disclose its nature in 1923 to the Ministry of Health Cancer Committee and in 1950 to the U. S. Food and Drug Administration. The *British Medical Journal* states on the basis of certain evidence that "it would be legitimate to suppose its principal ingredient is zinc chloride." Information received by them from the Tumor Therapy Committee suggested that there may be something else as well—possibly some form of colchicine both in the oral dose and in the mixture applied to the skin. The Committee also stated the treatment has not been shown to be free of serious toxic reactions.

### **Bertner Lectureship and Fellowship Opened . . .**

An annual lectureship covering the most important single advance in cancer research for the previous year has been established by the Bertner Foundation, Houston, Texas. The lectures will be delivered in the symposium on fundamental cancer research, which is sponsored each year by the University of Texas, M. D. Anderson Hospital for Cancer Research. A reciprocal exchange senior-fellowship program has also been established with the Memorial Center for Cancer and Allied Diseases, New York City. Each \$5,000 fellowship will be known as "The Jesse H. James Fellowship in Cancer Education Honoring Dr. E. W. Bertner." Further information regarding the lectureship and fellowship may be obtained from William G. Russell, Chairman, Education Committee, University of Texas, 2310 Baldwin Street, Houston.

### **Ewing and Delafield Hospitals Opened in N. Y. C. . . .**

Two new cancer hospitals, each with approximately 300 beds and built at a total cost of \$13,600,000, were opened this fall as the first two units of New York City's \$192,000,000 hospital-construction program. The James Ewing Hospital, at First Avenue between 67th and 68th Streets, is a functional unit of Memorial Center and is intended mainly for the city's indigent patients. The twelve-story institution is named for the famous cancer-research specialist who was director of Memorial Hospital for many years. The six-story Francis Delafield Hospital, at 163d Street and Fort Washington Avenue, is affiliated with Columbia-Presbyterian Medical Center and includes an outpatient department, research laborato-



ries, and a 2,000,000-volt roentgen-ray installation. This machine is the second of its type installed in New York City.

### **Re-establishing Continuity . . .**

Total gastric resection is too frequently followed by mechanical difficulties that cause the patient distress and require extensive modification of normal eating habits. In an effort to re-establish the continuity of the alimentary tract so it will more closely approximate normal organ relationships, Dr. Marshall Lee (U. of Cincinnati) reported at the Congress of the American College of Surgeons his animal experimental work in transposing the cecum and ascending colon into the upper abdomen and constructing a substitute gastric reservoir with this segment of the large bowel. The operation has been performed on one human patient with success.

# American Cancer Society Fellowships in Exfoliative Cytology

**Background**—At the Society's Symposium on Exfoliative Cytologic Diagnostic Techniques held in Boston in April, 1948, it was the opinion of the invited delegates that training facilities were urgently needed to train qualified pathologists and clinicians in teaching positions at approved institutions providing residency training in pathology as well as facilities for training technicians.

At the same time, the delegates recommended that the American Cancer Society proceed to engage the active interest and support of institutions and laboratories in setting up such training programs where the best training facilities appeared to be available. During the past year, ten laboratories actively participated in this program, and, at the present time, fellowships are available in thirteen institutions.

**Purpose**—To provide training in diagnostic techniques in exfoliative cytology for qualified pathologists. It is anticipated that trainees will not assume the role of teachers until sufficient personal experience and competence have been acquired.

**Awards**—Fellowships shall be awarded by institutions or laboratories designated by the Society to individuals on the basis of their past training and their intention to teach in their own laboratories diagnostic techniques in exfoliative cytology to interested pathologists, clinicians, and technicians.

**Eligibility of Applicant**—Applicants for Fellowships in Exfoliative Cytology of the American Cancer Society shall:

1. Be graduates of Class A Medical Schools of the United States, of its Territories, or of Canada
2. Be citizens of the United States
3. Be not over 50 years of age on the next birthday following commencement of Fellowship tenure
4. Have completed two years of post-graduate training in pathology
5. Conform in other respects to the requirements of the institution to which he applies

**Term of Fellowship**—Each Fellowship shall be awarded for a period of four months. Fellowship training may commence at any time convenient to the laboratory and to the Fellow. Such Fellowships may be subject to renewal.

**Stipends**—Stipends of \$140.00 per month shall be paid directly to Fellows by the Society. Modest grants are made available to the laboratory for equipment and overhead.

**Applications**—Individual applicants for Fellowships in Exfoliative Cytology shall apply directly to the Director of the laboratory where Fellowships are available. In no instance shall application be made directly to the American Cancer Society, Inc.

## FELLOWSHIPS AVAILABLE

Laboratory	Number	Director
Cornell University Medical College, New York, N. Y.	6	George N. Papanicolaou, M.D.
Jefferson Hospital, Philadelphia, Pa.	6	Lewis C. Scheffey, M.D.
New York Post-Graduate Hospital, New York, N. Y.	5	Locke L. Mackenzie, M.D.
University of Oregon Medical School, Portland, Ore.	2	Warren C. Hunter, M.D.
University of California Hospital, San Francisco, Calif.	2	Herbert F. Traut, M.D.
Michael Reese Hospital, Chicago, Ill.	2	Otto Saphir, M.D.
Hartford Hospital, Hartford, Conn.	2	Ralph E. Kendall, M.D.
Yale University School of Medicine, New Haven, Conn.	2	Samuel C. Harvey, M.D.
Washington University School of Medicine, St. Louis, Mo.	2	Lauren V. Ackermann, M.D.
Free Hospital for Women, Brookline, Mass.	1	Arthur T. Hertig, M.D.
Mayo Clinic, Rochester, Minn.	1	John R. McDonald, M.D.
University of Rochester, Rochester, N. Y.	1	Hannah T. Peters, M.D.
University of Georgia, Augusta, Ga.	1	H. E. Nieburgs, M.D.

smears is increasing accuracy and reducing technicians' searching time in cytological diagnosis. Polaroid's color-translating ultraviolet microscope continues to show exquisite detail of cells, and scientists are seeking micro-chemical or physical differences that may aid diagnosis. TUFTS is still intrigued by  $\beta$ -glucuronidase blood levels in cancer but is not convinced yet of the enzyme's value in screening or diagnosis.

Preliminary tests at TENNESSEE indicate that a simple sedimentation rate is about as accurate as some reported blood tests for cancer. Although some early skin cancers may register as positive, so do a variety of non-neoplastic diseases.

M. D. ANDERSON HOSPITAL (Houston, Texas) is trying to find out what a modified Kahn test might show in cancer.

GEORGE WASHINGTON investigators are exploring vitamin-A levels as an index to normal and abnormal endocrine function. They also are checking Swiss claims that the blood's ability to degrade pentose may be used as a cancer test, diagnostic and prognostic.

Fungus: Wuerthele-Caspe at RUTGERS, who first (1947) reported demonstrating the presence of specific micro-organisms in tumor cells, has isolated them from blood in cases of scleroderma, human cancer, Rous sarcoma, and mouse sarcoma 180. The organisms, related to mycobacteria, are morphologically similar, vary in shape and size, and exhibit several types. So far, efforts to isolate them from blood of normal people and patients with a variety of non-proliferative diseases have failed. Injected into animals, cultures produce pseudocaseous lesions and stimulate huge production of lymphocytes. The investigator has yet to establish whether the organisms are of primary or secondary significance in carcinogenesis.

Prognosis: YALE scientists, basing their measurements on the release of labeled desoxyribonucleic acid with cell destruction, now can calculate the longevity of cells.



Cancer cells outlive normal cells. The measure of their life span before and after treatment may give a yardstick of the effectiveness of therapy, diet, etc.

TULANE observes that a number of breast-cancer patients responding well to testosterone register a striking decrease in creatinine-creatinine ratio.

Immunology: INSTITUTE for CANCER RESEARCH (Philadelphia) scientists are conjugating carcinogens with proteins in an effort to develop a cancer-immune reaction. Others are doing classic work in perfecting nutrients that are completely chemically defined, thus laying the groundwork for biochemical observations of the future.

Basic: The low-temperature spectroscopy at MASS. INST. TECH. is yielding valuable data on the characterization, differentiation, and energy states of molecules of a variety of pyrimidine substitutes. Purines change little between room-temperature and low-temperature absorption spectra.

Weight: A preliminary study of 100 breast-cancer patients at MINNESOTA showed they had a slightly lower mean body weight than did 100 noncancerous out-patients paired with them for height and age. This eventually may challenge others' findings that fat people get more cancer than do skinny ones.

Surgery: Eliel, Pearson, and Rawson at MEMORIAL CENTER, N. Y., are reporting evidence that postoperative syndromes (apathy, lethargy, nervousness, weakness, occasional delirium, twitching, edema, metabolic alkalosis, etc.) may be due to potassium loss caused in part by adrenal hyperfunction from surgical trauma. They recommend administering potassium and possibly the phosphate ion early in the postoperative period to prevent the syndrome--unless dehydration and other contraindications are present.

Therapy: The MEDICAL COLLEGE of VIRGINIA is investigating the action of radiogold against various tumors.



## COMING MEDICAL MEETINGS

<b>Date</b>	<b>Association</b>	<b>City</b>	<b>Place</b>
1951			
April	World Medical Association Mid-year Council	Brussels, Belgium	
April 26-28	American Association of Patholo- gists and Bacteriologists	Cleveland	Auditorium
May 2-5	American Pediatric Society	Atlantic City	Convention Hall
May 21-24	American Urological Association	Chicago	
June 11-15	American Medical Association, Annual Session	Atlantic City	Convention Hall



